

5/11/98
U.S. PTO

Atty Dkt 15002
Client No. 2302-1393
PATENT

1611/

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on May 7, 1998.

5/7/98
Date

Patricia K. James
Signature

2921

4
MW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE 2900

In Re Application of:

BARCHFIELD et al.

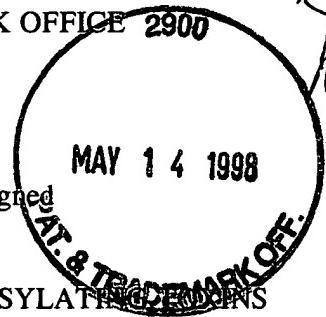
Serial No.: 09/044,696

Group Art Unit: Unassigned

Filing Date: March 18, 1998

Examiner: Unassigned

Title: DETOXIFIED MUTANTS OF BACTERIAL ADP-RIBOSYLATING ENZYMES
AS PARENTERAL ADJUVANTS



TRANSMITTAL LETTER

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an Information Disclosure Statement, including a Form PTO-1449 and copies of the cited references. It is believed that no fee is due.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: 5/7/98

By: Roberta L. Robins
Roberta L. Robins
Registration No. 33,208

ROBINS & ASSOCIATES
90 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 325-7812
Facsimile: (650) 325-7823



Atty Dkt 1393.002
Client No. 2302-1393
PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on May 7, 1998.

5/7/98
Date

Patricia K. Adams
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

BARCHFIELD et al.

Serial No.: 09/044,696

Group Art Unit: Unassigned

Filing Date: March 18, 1998

Examiner: Unassigned

Title: DETOXIFIED MUTANTS OF BACTERIAL ADP-RIBOSYLATING
TOXINS AS PARENTERAL ADJUVANTS

**INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. § 1.97**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. Copies of the information and completed PTO-1449 forms are submitted herewith. The Examiner is respectfully requested to make this information of official record in the application. The information includes:

International Publication No. WO 92/19265, published November 12, 1992;
International Publication No. WO 93/13202, published July 8, 1993;
International Publication No. WO 95/17211, published June 29, 1995;
Agren et al., "Genetically Engineered Nontoxic Vaccine Adjuvant That Combines B Cell Targeting with Immunomodulation by Cholera Toxin A1 Subunit," *J. Immunol.* 158:3936-3946 (1997);

Akhiani et al., "Effect of Cholera Toxin on Vaccine-Induced Immunity and Infection in Murine Schistosomiasis Mansoni," *Infection and Immunity* 61(11):4919-4924 (1993);

Clements et al., "Adjuvant Activity of *Escherichia coli* Heat-Labile Enterotoxin and Effect on the Induction of Oral Tolerance in Mice to Unrelated Protein Antigens," *Vaccine* 6:269-277 (1988);

Elson, "Cholera Toxin as a Mucosal Adjuvant," *Mucosal Vaccines* Chapter 4:59-72 (1996);

Elson, "Cholera Toxin and its Subunits as Potential Oral Adjuvants," *Curr. Top. Microbiol. Immunol.* 146:29-33 (1989);

Elson et al., "A Lavage Technique Allowing Repeated Measurement of IgA Antibody in Mouse Intestinal Secretions," *Journal of Immunological Methods* 67:101-108 (1984);

Elson et al., "Generalized Systemic and Mucosal Immunity in Mice After Mucosal Stimulation With Cholera Toxin," *The Journal of Immunology* 132(6):2736-2741 (1984);

Elson et al., "Ir Gene Control of the Murine Secretory IgA Response to Cholera Toxin," *Eur. J. Immunol.* 17:425-428 (1987);

Elson et al., "Cholera Toxin Feeding Did Not Induce Oral Tolerance in Mice and Abrogated Oral Tolerance to an Unrelated Protein Antigen," *The Journal of Immunology* 133(6):2892-2897 (1984);

Gizurarson et al., "The Effect of Cholera Toxin and Cholera Toxin B Subunit on the Nasal Mucosal Membrane," *Vaccine* 9:825-832 (1991);

Glenn et al., "Skin Immunization Made Possible by Cholera Toxin," *Nature* 391:851 (1998);

Hirabayashi et al., "Involvement of Antigen-Presenting Cells in the Enhancement of the *In Vitro* Antibody Responses by Cholera Toxin B Subunit," *Immunology* 75:493-498 (1992);

Hirabayashi et al., "Comparison of Intranasal Inoculation of Influenza HA Vaccine Combined With Cholera Toxin B Subunit With Oral or Parenteral Vaccination," *Vaccine* 8:243-248 (1990);

Hirabayashi et al., "H-2-Unrestricted Adjuvant Effect of Cholera Toxin B Subunit on Murine Antibody Responses to Influenza Virus Haemagglutinin," *Immunology* 72:329-335 (1991);

Holmgren et al., "Cholera Toxin and Cholera B Subunit as Oral-Mucosal Adjuvant and Antigen Vector Systems," *Vaccine* 11:1179-1183 (1993);

Kikuta et al., "Cross-Protection Against Influenza B Type Virus Infection by Intranasal Inoculation of the HA Vaccines Combined with Cholera Toxin B Subunit," *Vaccine* 8:595-599 (1990);

Lycke et al., "The Adjuvant Effect of *Vibrio Cholerae* and *Escherichia Coli* Heat-Labile Enterotoxins is Linked to Their ADP-Ribosyltransferase Activity," *Eur. J. Immunol.* 22:2277-2281 (1992);

Lyke et al., "Strong Adjuvant Properties of Cholera Toxin on Gut Mucosal Immune Responses to Orally Presented Antigens," *Immunology* 59:301-308 (1986);

Nathaniel F. Pierce, "The Role of Antigen Form and Function in the Primary and Secondary Intestinal Immune Responses to Cholera Toxin and Toxoid in Rats," *J. Exp. Med.* 148:195-206 (1978);

Pierce et al., "Cellular Kinetics of the Intestinal Immune Response to Cholera Toxoid in Rats," *J. Exp. Med.* 142:1550-1563 (1975);

Snider, "The Mucosal Adjuvant Activities of ADP-Ribosylating Bacterial Enterotoxins," *Critical Review in Immunology* 15(3&4):317-348 (1995);

Tamura et al., "Cross-Protection Against Influenza Virus Infection Afforded By Trivalent Inactivated Vaccines Inoculated Intranasally With Cholera Toxin B Subunit," *The Journal of Immunology* 149(3):981-988 (1992);

Tamura et al., "Protection Against Influenza Virus Infection by a Two-Dose Regimen of Nasal Vaccination Using Vaccines Combined With Cholera Toxin B Subunit," *Vaccine* 7:314-320 (1989);

Tamura et al., "Enhancement of Protective Antibody Responses by Cholera Toxin B Subunit Inoculated Intranasally With Influenza Vaccine," *Vaccine* 7:257-262 (1989);

Tamura et al., "Protection Against Influenza Virus infection by Vaccine Inoculated Intranasally With Cholera Toxin B Subunit," *Vaccine* 6:409-413 (1988);

Tamura et al., "Effectiveness of Cholera Toxin B Subunit as an Adjuvant for Nasal Influenza Vaccination Despite Pre-Existing Immunity to CTB," *Vaccine* 7:503-505 (1989);

Van Der Heijden et al., "Manipulation of Intestinal Immune Responses Against Ovalbumin by Cholera Toxin and its B Subunit in Mice," *Immunology* 72:89-93 (1991);

Wilson et al., "Adjuvant Effect of Cholera Toxin on the Mucosal Immune Response to Soluble Proteins, Differences Between Mouse Strains and Protein Antigens," *Scand. J. Immunol.* 29:739-745 (1989); and

Wilson et al., "Adjuvant Action of Cholera Toxin and Pertussis Toxin in the Induction of IgA Antibody Response to Orally Administered Antigen," *Vaccine* 11(2):113-115 (1993).

This Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are

Atty Dkt No. 1393.002
USSN: 09/044,696
PATENT

accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

Date: 5/1/98

By: Roberta L. Robins
Roberta L. Robins
Registration No. 33,208

ROBINS & ASSOCIATES
90 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 325-7812
Fax: (650) 325-7823